

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re patent of Andrew Fire et al. No. 6,506,559 Issued: January 14, 2003  
For: Genetic inhibition by double-stranded RNA

Submission of Prior Art Under 37 C.F.R. 1.501

Honorable Commissioner for Patents P.O. Box 1450 Alexandria, VA  
22313-1450

Sir:

This is an anonymous Submission of Prior Art pursuant to 35 U.S.C. 301 and 37 C.F.R. 1.501. U.S. Patent No. 5,597,697 to Diamond, issued January 28, 1997 ("the Diamond patent") is hereby cited to the file of U.S. Patent No. 6,506,559 to Fire et al., issued January 14, 2003 ("the Fire patent"). A copy of the Diamond patent is enclosed, for which entry is requested.

The Diamond patent is relevant to at least claim 1 of the Fire patent. The Diamond patent discloses a method for inhibiting the expression of a target gene in which an RNA-dependent RNA polymerase acts on an RNA transcript of the target gene to form a double-stranded RNA molecule. Double-stranded RNA ("dsRNA") is an inducer of RNA silencing. The Diamond patent also discloses embodiments in which the resulting dsRNA molecule is digested by an RNase III enzyme. The dsRNA products of the RNase III digestion are, today, called siRNAs (for "silencing RNAs") and are known to mediate RNA silencing in cells, including plant and animal cells.

Certificate of Service and Duplicate Copy of Submission for Fire et al.

The anonymous submitter hereby certifies that a true and correct copy of the foregoing "Submission of Prior Art" was mailed on November 22, 2004 by first-class mail, postage-paid to the correspondent attorney of Fire et al.:

Morgan, Lewis & Bockius, LLP  
Patent Department  
1111 Pennsylvania Ave., N.W.  
Washington, D.C. 20004

**In view of the anonymity of this submission, a duplicate copy is also enclosed in the event that direct service by the United States Patent and Trademark Office on Fire et al. is deemed appropriate.**



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